What is claimed is:

1. A variant antithrombin III, comprising a substitution at position P2, wherein the substitution at P2 is a P.

2. A variant antithrombin III, comprising a substitution at position P3, wherein the substitution at P3 is a D, E, H, K, L, P, Q, R, W, or Y.

3. A variant antithrombin III, comprising a substitution at position P4, wherein the substitution at P4 is a L, N, Q, or V.

4. A variant antithrombin III, comprising one substitution at either position P3 and P4, wherein the substitution at P3 is D, E, H, K, L, P, Q, R, W, or Y, and wherein the substitution at P4 is L, N, Q, V, or W, and at least one substitution at P2, P5, P6, P7, and P8, wherein the substitution at P2 is P, P5 is E, F, G, or P, wherein the substitution at P6 is E, G, L, or T, wherein the substitution at P7 is E or Q, and wherein the substitution at P8 is E.

5. A variant antithrombin III, comprising two substitutions at P3 and P4, wherein the substitution at P3 is D, E, G, H, I, K, L, N, P, Q, R, S, W, or Y, and wherein the substitution at P4 is L, N, Q, V, or W.

6. A variant antithrombin III, comprising two substitutions at either position P3 and P4, wherein the substitution at P3 is D, E, H, K, L, P, Q, R, W, or Y, and wherein the substitution at P4 is A, F, G, L, N, P, Q, V, or W.

7. A variant antithrombin III, comprising two substitutions at P2, P3 and P4, wherein the substitution at P2 is P, wherein the substitution at P3 is D, E, G, H, I, K, L, N, P, Q, R, S, W, or Y, and wherein the substitution at P4 is A, F, G, L, N, P, Q, V, or W.

8. A variant antithrombin III, comprising a substitution at P2, P3 and P4, wherein the substitution at P2 is P, wherein the substitution at P3 is D, E, H, K, L, P, Q, R, S, W, or Y, and wherein the substitution at P4 is L, N, Q, V, or W.

9. A variant antithrombin III, comprising one substitution at P3 and P4, wherein the substitution at P3 is D, E, H, K, L, P, Q, R, S, W, or Y, and wherein the substitution at P4 is L, N, Q, V, or W, and wherein P2 is P.

10. A variant antithrombin III, comprising one substitution at P5, wherein the substitution at P5 is D, H, N, Q, R, S, T, V, W, or Y.

11. A variant antithrombin III, comprising one substitution at P7, wherein the substitution at P7 is F, H, L, S, T, or V.

12. A variant antithrombin III, comprising two substitutions at P5 or P7, wherein the

substitution at P5 is D, H, N, Q, R, S, T, V, W, or Y and wherein the substitution at P7 is F, H, L, S, T, or V.

13. A variant Antithrombin III (ATT), comprising two substitutions at position P2, P3, P4, P5, P6, or P7, wherein a first substitution at P2 is P, and wherein the second substitution at P3 can be D, E, G, H, I, K, L, N, P, Q, R, S, W, or Y, wherein the second substitution at P4 can be A, F, G, L, N, P, Q, V, or W, wherein the second substitution at P5 can be D, E, F, G, H, K, N, P, Q, R, S, T, or V, wherein the substitution at P6 can be E, G, L, or T, and wherein the second substitution at P7 can be E, F, H, L, Q, S, T, or V.

14. A variant Antithrombin III (ATT), comprising three substitutions at position P2, P3, P4, P5, P6, or P7, wherein a first substitution at P2 is P, and wherein the second or third substitution at P3 can be D, E, G, H, I, K, L, N, P, Q, R, S, W, or Y, wherein the second or third substitution at P4 can be A, F, G, L, N, P, Q, V, or W, wherein the second or third substitution at P5 can be D, E, F, G, H, K, N, P, Q, R, S, T, or V, wherein the substitution at P6 can be E, G, L, or T, and wherein the second or third substitution at P7 can be E, F, H, L, Q, S, T, or V.

15. A variant Antithrombin III (ATT), comprising four substitutions at position P2, P3, P4, P5, P6, or P7, wherein a first substitution at P2 is P, and wherein the second, third or fourth substitution at P3 can be D, E, G, H, I, K, L, N, P, Q, R, S, W, or Y, wherein the second, third or fourth substitution at P4 can be A, F, G, L, N, P, Q, V, or W, wherein the second, third or fourth substitution at P5 can be D, E, F, G, H, K, N, P, Q, R, S, T, or V, wherein the substitution at P6 can be E, G, L, or T, and wherein the second, third or fourth substitution at P7 can be E, F, H, L, Q, S, T, or V.

16. A variant Antithrombin III (ATT), comprising five substitutions at position P2, P3, P4, P5, P6, or P7, wherein a first substitution at P2 is P, and wherein the second, third, fourth, or fifth substitution at P3 can be D, E, G, H, I, K, L, N, P, Q, R, S, W, or Y, wherein the second, third, fourth, or fifth substitution at P4 can be A, F, G, L, N, P, Q, V, or W, wherein the second, third, fourth, or fifth substitution at P5 can be D, E, F, G, H, K, N, P, Q, R, S, T, or V, wherein the substitution at P6 can be E, G, L, or T, and wherein the second, third, fourth, or fifth at P7 can be E, F, H, L, Q, S, T, or V.

17. A variant Antithrombin III (ATT), comprising two substitutions at position P2, P3, P4, P5, or P7, wherein a first or second substitution at P2 can be P, wherein the first or second substitution at P3 can be D, E, H, K, L, P, Q, R, W, or Y, wherein the first or second substitution at P4 can be L, N, Q, V, or W, wherein the first or second substitution at P5 can be D, H` K, N, Q, R, S, T, or V, and wherein the first or second substitution at P7 can be F, H, L, S, T, or V.

18. A variant Antithrombin III (ATT), comprising three substitutions at position P2, P3,

P4, P5, or P7, wherein a first, second or third substitution at P2 is P, and wherein the first, second or third substitution at P3 can be D, E, G, H, I, K, L, N, P, Q, R, S, W, or Y, wherein the first, second or third substitution at P4 can be A, F, G, L, N, P, Q, V, or W, wherein the first, second or third substitution at P5 can be D, H` K, N, Q, R, S, T, or V, and wherein the first, second or third substitution at P7 can be F, H, L, S, T, or V.

19. A variant Antithrombin III (ATT), comprising four substitutions at position P2, P3, P4, P5, or P7, wherein the first, second, third or fourth substitution at P2 is P, and wherein the first, second, third or fourth substitution at P3 can be D, E, G, H, I, K, L, N, P, Q, R, S, W, or Y, wherein the first, second, third or fourth substitution at P4 can be A, F, G, L, N, P, Q, V, or W, wherein the first, second, third or fourth substitution at P5 can be D, H` K, N, Q, R, S, T, or V, and wherein the first, second, third or fourth substitution at P7 can be F, H, L, S, T, or V.

20. A variant Antithrombin III (ATT), comprising five substitutions at position P2, P3, P4, P5, or P7, wherein a first substitution at P2 is P, and wherein the first, second, third or fourth substitution at P3 can be D, E, G, H, I, K, L, N, P, Q, R, S, W, or Y, wherein the first, second, third or fourth substitution at P4 can be A, F, G, L, N, P, Q, V, or W, wherein the first, second, third or fourth substitution at P5 can be D, H` K, N, Q, R, S, T, or V, and wherein the first, second, third or fourth at P7 can be F, H, L, S, T, or V.

21. The variant ATIII of claim 15, wherein there is an L at P6, E at P5, A at P4 and Q at P3 and has increased protease resistance and retains thrombin inhibition activity.

22. The variant ATIII of claim 15, wherein there is an L at P6, E at P5, A at P4 and Q at P3 and has increased protease resistance and retains fXa inhibition activity.

23. The variant ATIII of claim 15, wherein there is an L at P6, E at P5, A at P4 and Y at P3 and has increased protease resistance and retains thrombin inhibition activity.

24. The variant ATIII of claim 15, wherein there is an L at P6, E at P5, A at P4 and Y at P3 and has increased protease resistance and retains fXa inhibition activity.

25. The variant ATIII of claim 15, wherein there is an L at P6, E at P5, A at P4 and H at P3 and has increased protease resistance and retains thrombin inhibition activity.

26. The variant ATIII of claim 15, wherein there is an L at P6, E at P5, A at P4 and H at P3 and has increased protease resistance and retains fXa inhibition activity.

27. The variant ATIII of claim 15, wherein there is an L at P6, E at P5, A at P4 and R at P3 and has increased protease resistance and retains thrombin inhibition activity.

28. The variant ATIII of claim 15, wherein there is an L at P6, E at P5, A at P4 and R at P3

and has increased protease resistance and retains fXa inhibition activity.

29. The variant ATIII of claims 1-20, wherein the variant ATIII has a combined activity greater than or equal to plasma ATIII in a coupled assay.

30. The variant ATIII of claim 29,wherein the ATIII retains base thrombin inhibition activity of at least 5%.

31. The variant ATIII of claim 29,wherein the ATIII retains base thrombin inhibition activity of at least 50%.

32. The variant ATIII of claim 29,wherein the ATIII retains base thrombin inhibition activity of at least 95%.

33. The variant ATIII of claim 29,wherein the the variant ATIII produce a predicted half life of thrombin at 60 minutes after a bolus administration to a subject that is greater than or equal to .9 the half life following a plasma ATIII administration.

34. The variant ATIII of claim 29,wherein the the variant ATIII produce a predicted half life of thrombin at 60 minutes after a bolus administration to a subject that is greater than or equal to .01 the half life following a plasma ATIII administration.

35. The variant ATIII of claim 29,wherein the the variant ATIII produce a predicted half life of thrombin activity at 60 minutes after a bolus administration to a subject that is greater than or equal to .0001 the half life following a plasma ATIII administration.

36. The variant ATIII of claim 29, wherein the variant antithrombin III has a combined activity greater than or equal to 2 times the activity of plasma ATIII in a coupled assay.

37. The variant antithrombin III of claim29, wherein the variant antithrombin III has a combined activity greater than or equal to 5 times the activity of plasma ATIII in a coupled assay.

38. The variant antithrombin III of claim 29, wherein the variant antithrombin III has a combined activity greater than or equal to 10 times the activity of plasma ATIII in a coupled assay.

39. The variant antithrombin III of claim 29, wherein the variant antithrombin III has an increased protease resistance greater than or equal to the protease resistance of plasma ATIII.

40. The variant antithrombin III of claim 29, wherein the variant antithrombin III has an increased human nuetrophil elastase resistance greater than or equal to the protease resistance of plasma ATIII.

41. The variant antithrombin III of claim 29, wherein the variant antithrombin III has an increased cathepsin G resistance greater than or equal to the protease resistance of plasma ATIII.

42. The variant antithrombin III of claim 29, wherein the variant antithrombin III has at least 70% identity to SEQ ID NO:93.

43. The variant ATIII of claims 1-20, wherein the variant ATIII retains increased protease resistance and retains observable anti-thrombin activity.

44. The variant ATIII of claim 43,wherein the ATIII retains base thrombin inhibition activity of at least 5%.

45. The variant ATIII of claim 43,wherein the ATIII retains base thrombin inhibition activity of at least 50%.

46. The variant ATIII of claim 43,wherein the ATIII retains base thrombin inhibition activity of at least 95%.

47. The variant ATIII of claims 43 wherein the activity is with respect to plasma ATIII.

48. The variant of claim 43,wherein the the variant ATIII produce a predicted half life of thrombin at 60 minutes after a bolus administration to a subject that is greater than or equal to .9 the half life following a plasma ATIII administration.

49. The variant of claim 43,wherein the the variant ATIII produce a predicted half life of thrombin at 60 minutes after a bolus administration to a subject that is greater than or equal to .01 the half life following a plasma ATIII administration.

50. The variant of claim 43,wherein the the variant ATIII produce a predicted half life of thrombin activity at 60 minutes after a bolus administration to a subject that is greater than or equal to .0001 the half life following a plasma ATIII administration.

51. The variant ATIII of claims 1-20, wherein the variant ATIII retains increased protease resistance and retains observable anti factor fXa activity.

52. The variant ATIII of claims 1-20, wherein the variant ATIII retains increased protease resistance and retains observable anti-thrombin and anti factor fXa activity.

53. The variant ATIII of claims 1-20, wherein the variant ATIII retains increased protease resistance and has increased anti-thrombin activity.

54. The variant ATIII of claims 1-20, wherein the variant ATIII retains increased protease resistance and has increased anti factor fXa activity.

55. The variant ATIII of claims 1-20, wherein the variant ATIII retains increased protease resistance and has increase anti-thrombin and anti factor fXa activity.

56. The variant ATIII of claims 1-20, wherein the variant comrpises increased protease

resistance and retains greater observable anti-thrombin activity than observable anti-fXa activity.

57. The variant ATIII of claims 1-20, wherein the variant comprises increased protease resistance and retains greater observable anti-fXa activity than observable anti-thrombin and activity.

58. The variant ATIII of claims 1-20, wherein the variant is cleaved by a protease at less than or equal to 75% of the rate of plasma ATIII.

59. The variant ATIII of claims 1-20, wherein the variant is cleaved by a protease at less than or equal to 25% of the rate of plasma ATIII.

60. The variant ATIII of claims 1-20, wherein the variant is cleaved by a protease at less than or equal to 0.1% of the rate of plasma ATIII.

61. A method of inhibiting septic disseminated intravascular coagulation by administrating the ATIII of claims 1-20 to a subject having septic disseminated intravascular coagulation.

62. A method of reducing sepsis, comprising administering the ATIII of claims 1-20 to a subject having sepsis.

63. A method of inhibiting sepsis induced shock comprising administering the ATIIIof claims 1-20 to a subject.

64. A method of making the variant ATIII of claims 1-20, comprising linking in an operative way a nucleic acid molecule encoding a variant ATIII comprising a sequence having 80% identity to a sequence set forth in SEQ ID NO:77, and a sequence controlling the expression of the nucleic acid.

65. A method of making the variant ATIII of claims 1-20, comprising linking in an operative way a nucleic acid molecule encoding a protein set forth in SEQ ID NO:77 wherein the nucleic acid sequence comprises a sequence that hybridizes under stringent hybridization conditions to a sequence set forth SEQ ID NO:79, or a degenerate variant thereof, and a sequence controlling the expression of the nucleic acid.

66. A cell comprising the variant ATIII of claims 1-20.

67. A non-human animal comprising the variant ATIII of claims 1-20.

68. The non-human animal of claim 67, wherein the animal is a non-human mammal.

69. A non-human animal comprising the cell of claim 66.

70. The non-human animal of claim 69, wherein the animal is a non-human mammal.

71. A cell produced by the process of transforming the cell with any of the disclosed

nucleic acids of claims 64 or 65.

72. A cell produced by the process of administering the variant ATIII of claims 1-20.

73. A non-human animal produced by administering any of the variant ATIIIs of claims 1-20.

74. A non-human animal produced by administering the cell of claim 73.